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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 09/423,698 | 02/10/2000 | ODILE LEROY | 99-849-A | 7060 |

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| EXAMINER | |
|---|---|
| DUFFY, PATRICIA ANN | |
| ART UNIT | PAPER NUMBER |
| 1645 | |

| MAIL DATE | DELIVERY MODE |
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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/423,698 | LEROY, ODILE | |
| | Examiner | Art Unit | |
| | Patricia A. Duffy | 1645 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *12 November 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-7 and 12-31* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7 and 12-31* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *11/08*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## RESPONSE TO AMENDMENT

The amendment filed 11-12-08 has been entered into the record. Claims 1-7 and 12-31 are pending and are under examination.

The text of Title 35 of the U.S. Code not reiterated herein can be found in the previous office action.

### *Rejections Withdrawn*

The rejection of claims 1, 2, 4, 6, 7 and 14 under 35 U.S.C. 103(a) as being unpatentable over Ahman et al (Pediatr. Infect. Dis. J. 15:134-9, 1996) in view of Anderson et al (J. Pediatr. 128:649-53, 1996) is withdrawn based on the amendment to the claims.

### *Rejections Maintained*

Claims 1-7 and 12-31 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chu et al (Infection and Immunity, 40(1):245-256, April 1983) in view of Merck and Co. Inc. (EP 0497 525, May 8, 1992) is maintained for reasons made of record and herein.

Applicant's arguments have been carefully considered. Applicants argue that the combination is not obvious because the prior art provides not teachings, suggestion or recognition that the amount of carrier protein could be controlled by dose. This is not persuasive; it was known at the time of the invention that the type of carrier and amount used, and the ratio of carbohydrate to protein were factors that influenced the immunogenicity of conjugate preparations (see Klein et al (Microbial Drug Resistance, 1(1):49-58, 1995) at page 53, Table 4.) Thus, it was known that the amount of carrier protein used could affect the immunogenicity of the conjugate preparations. The identity of effective of carrier proteins was articulated by the art. The polysaccharides were articulated by the art, the means of conjugation was known to the art and the effect of carrier proteins were known to the art. Therefore the selection of carrier proteins, their dose and the ratio of polysaccharide to carrier proteins and combination of different

carrier proteins is well with the skilled artisans grasp. It is well settled that "discovery of an optimum value of a result effective variable in a known process is ordinarily within the skill of the art." *In re Boesch,* 617 F.2d 272, 276, 205 USPQ 215, 219 (CCPA 1980). *See also Merck & Co. v. Biocraft Labs. Inc.,* 874 F.2d 804, 809, 10 USPQ2d 1843, 1847-48 (Fed. Cir. 1989) (determination of suitable dosage amounts in diuretic compositions considered a matter of routine experimentation and therefore obvious). As the dose of carrier protein and the ratio of polysaccharide to carrier protein were known to affect immunogenicity, it would have been obvious to optimize the doses of the chosen carrier proteins, Dt and Tt and any of the others articulated by the art. Applicants argue that the art was silent with respect to combining different carrier proteins. This is simply not true, the use of multiple carrier proteins in the same composition was known to the art well prior to Applicants filing date (Klein et al (Microbial Drug Resistance, 1(1):49-58, 1995; already of record) which teaches "At the present time, all of the vaccine manufactures are aiming to produce pneumococcal conjugate vaccines that contain between seven and nine serotypes conjugated to one or several different carrier proteins." Applicants argue that combination of Dt and Tt is unbovious because of the Finnish and Israeli studies showing decreased anit-Hib antibody response with increase Dt and Tt load. This is not persuasive, because Applicants claims are not so limited and the interference occurred at a total Tt or Dt dose as recited in the claims (1-10 ug of Dt or Tt). As such, the claims do not provide for decreased interference as argued and there is no evidence that any of the formulations when combined with the HiB vaccine provides for decreased interference. Dose of carrier protein is a known results effected variable in the conjugate art. Applicants argue that the office has not established that ere are a finite number of identified and predictable solutions. This is not persuasive because the carrier proteins Dt and Tt were known to the art and successfully used as a carrier in conjugate vaccines. Applicants argue that the compositions are not obvious because it took 100 years to develop such vaccines. This is not persuasive because it was known to the art that a

commercially successful 23-valent pneumococcal vaccine was on the market and the high costs in developing and manufacturing multivalent conjugate vaccines would delay their development by manufacturers (Klein et al supra, page 52, column 2). Applicants argue that the office has indicated combination of any random collection of antigen and expect to observe a safe and useful immune response. This is not persuasive because it is not random combination of any antigen it is a combination of known protective antigens. Applicants assert numerous difficulties and unpredictability in the art with respect to combination of antigens. This is not persuasive because the 23-valent vaccine was known to be effective and Applicants have provided no evidence of the unpredictability in the art as it relates to negative interference the combination of the 23-valent polysaccharide antigens. Further, should Applicants provide such evidence then they should be prepared to limit the compositions to the disclosed embodiments because of the alleged unpredictability of negative interference. Applicants argue that the combination of Chu and the '525 application does not provide for the combination of Dt and Tt in the same dose. This is not persuasive; the combination of multiple carrier proteins as articulated by Merck and Co. Inc ('525 application) is obvious. Applicants argue that the issue is that Applicants discovered that that pneumococcal polysaccharides could be conjugated to both Dt and Tt (this is taught by Merck and Co Inc) and that the loads of Dt and Tt could be reduced therefore avoiding the effects of carrier suppression. This is not again not persuasive, the use of Dt and Tt as carriers for conjugate vaccine was known in the art and the dosage of the carrier protein was a known variable affecting the immunogenicity of the conjugate and although the art does not teach the low total dosages of Dt and Tt, the dose of the carrier protein is a results effected variable known to the skilled artisan.

Claims 1-7 and 12-31 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ahman et al (Pediatr. Infect. Dis. J. 15:134-9, 1996) in view of Anderson et al (J. Pediatr. 128:649-53, 1996) as applied to claims 1, 2, 4, 6, 7 and 14 supra and further in view of

Merck and Co. Inc. (EP 0497 525, May 8, 1992) is maintained for reasons set forth in the office action mailed 5-13-08.

Applicants essentially reiterate the arguments of record. The rejection is maintained for reasons set forth in the non-final rejection of 5-13-08 and herein. The combination teaches all the carriers and polysaccharides, exemplifies with two different carrier proteins and it would have been obvious to combine different conjugates conjugated to the recited different carriers identified by Merck and Co. Inc. As set forth supra, the number of known carrier proteins were articulated by the art. The polysaccharides were articulated by the art, the means of conjugation was known to the art and the effect of carrier proteins were known to the art. Therefore the selection of carrier proteins, their dose and the ratio of polysaccharide to carrier proteins are well with the skilled artisans grasp. It is well settled that "discovery of an optimum value of a result effective variable in a known process is ordinarily within the skill of the art." *In re Boesch,* 617 F.2d 272, 276, 205 USPQ 215, 219 (CCPA 1980). *See also Merck & Co. v. Biocraft Labs. Inc.,* 874 F.2d 804, 809, 10 USPQ2d 1843, 1847-48 (Fed. Cir. 1989) (determination of suitable dosage amounts in diuretic compositions considered a matter of routine experimentation and therefore obvious). As the dose of carrier protein and the ratio of polysaccharide to carrier protein were known to affect immunogenicity, it would have been obvious to optimize the doses of the chosen carrier proteins, Dt and Tt and any of the others articulated by the art.

***New Rejections Based on Amendment***

Claims 1-7, 12-15 and 24 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claim has been amended to recite a composition comprising "one or more dosages of a vaccine" . This limitation is not found at pages 5 or 8 as indicated in Applicants response. This issue is best resolved by Applicants pointing to the specification by page and line number where written description support can be found.

***Status of Claims***

Claims 1-7 and 12-31 stand rejected.

***Conclusion***

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Patricia A. Duffy whose telephone number is 571-272-0855. The examiner can generally be reached on M-Th 7:30 am - 6:00 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's Supervisors, Robert Mondesi can be reached at 571-272-0956.

The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

/Patricia A. Duffy/
Primary Examiner